solution 1. Combine the buffer extractives in a suitable volumetric flask and dilute to volume with solution 1. Remove an aliquot, add sufficient hydrochloric acid so that the amount of acid in the final solution will be the same as in the reference concentration of the working standard and further dilute with solution 1 to the reference concentration of 1.0 unit of bacitracin per milliliter (estimated).

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(3) of that section.

(3) *Moisture.* Proceed as directed in § 436.201 of this chapter.

(4) *Metal particles.* Proceed as directed in § 436.206 of this chapter.

[42 FR 27230, May 27, 1977, as amended at 50 FR 19920, May 13, 1985]

§ 448.313 Bacitracin zinc ophthalmic dosage forms.

§ 448.313a Bacitracin zinc-polymyxin B sulfate ophthalmic ointment.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Bacitracin zinc-polymyxin B sulfate ophthalmic ointment contains in each gram 500 units of a bacitracin and 10,000 units of polymyxin B in a suitable and harmless ointment base. Its bacitracin content is satisfactory if it is not less than 90 percent and not more than 130 percent of the number of units of bacitracin that it is represented to contain. Its polymyxin B content is satisfactory if it is not less than 90 percent and not more than 130 percent of the number of units of polymyxin B that it is represented to contain. It is sterile. Its moisture content is not more than 0.5 percent. It passes the test for metal particles. The bacitracin zinc used conforms to the standards prescribed by § 448.13a(a)(1). The polymyxin B sulfate used conforms to the standards prescribed by § 448.30a(a)(1).

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(*a*) The bacitracin zinc used in making the batch for potency, loss on drying, pH, zinc content, and identity.

(*b*) The polymyxin B sulfate used in making the batch for potency, loss on drying, pH, and identity.

(*c*) The batch for bacitracin content, polymyxin B content, sterility, moisture, and metal particles.

(ii) Samples required:

(*a*) The bacitracin zinc used in making the batch: 10 packages, each containing approximately 1.0 gram.

(*b*) The polymyxin B sulfate used in making the batch: 10 packages, each containing approximately 1.0 gram.

(*c*) The batch:

(*1*) For all tests except sterility: A minimum of 17 immediate containers.

(*2*) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1) *Potency*—(i) *Bacitracin content.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Place an accurately weighed representative portion of the sample into a separatory funnel containing approximately 50 milliliters of peroxide-free ether. Shake the sample and ether until homogeneous. Add 20 to 25 milliliters of 0.01*N* hydrochoric acid and shake well. Allow the layers to separate. Remove the acid layer and repeat the extraction procedure with each of three more 20- to 25-milliliter quantities of 0.01*N* hydrochloric acid. Combine the acid extractives in a suitable volumetric flask and dilute to volume with 0.01*N* hydrochloric acid. (If the bacitracin content is less than 100 units per milliliter in 0.01*N* hydrochloric acid, add sufficient additional hydrochloric acid to each concentration of the standard response line so that each standard solution contains the same amount of acid as the final sample solution.) Remove an aliquot and further dilute with solution 1 to the reference concentration of 1.0 unit of bacitracin per milliliter (estimated).

(ii) *Polymyxin B content.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Place an accurately weighed representative portion of the sample into a separatory funnel containing approximately 50 milliliters of peroxide-free